Supplemental Data Appendix

Figures 1a-d. Forrest plots comparing R-CHOP vs IIC stratified for various baseline characteristics in the entire cohort (n=104). None of the baseline characteristics were associated with benefit of IIC over R-CHOP or vice versa.

Abbreviations: sm-IPI, stage modified international prognostic index; LDH, lactate dehydrogenase, DLBCL, diffuse large B-cell lymphoma; HGBL, high-grade B-cell lymphoma; GCB, germinal center B-cell; DHL, double-hit lymphoma; RT, radiation therapy; CNS, central nervous system; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone; IIC, intensive immunochemotherapy.

Figure 1a. Forrest plot comparing CR rates in the R-CHOP vs IIC group stratified by various baseline parameters. There was no benefit of IIC over R-CHOP or vice versa in any sub-group.

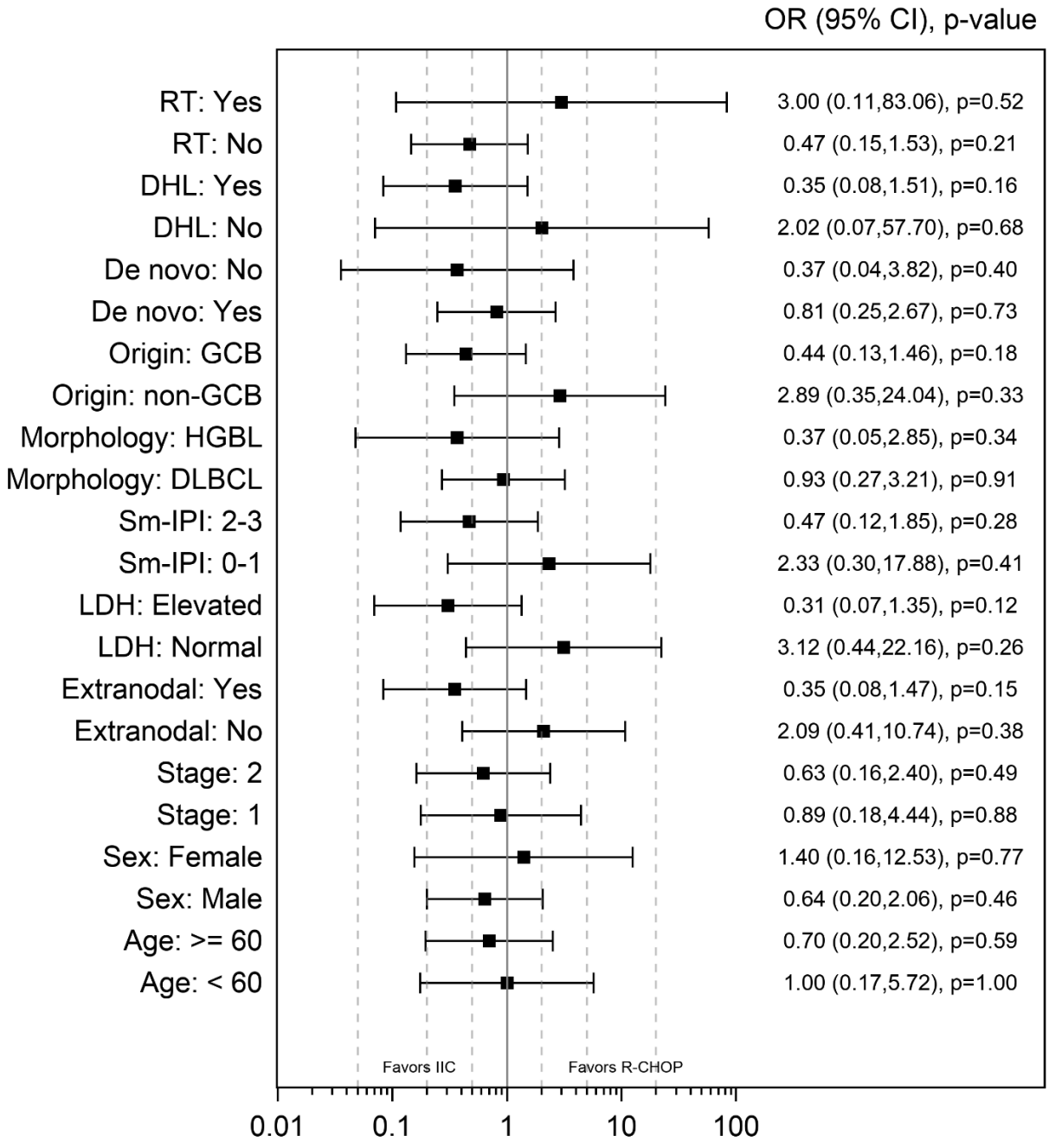


Figure 1b. Forrest plot comparing ORR rates in the R-CHOP vs IIC group stratified by various baseline parameters. There was no benefit of IIC over R-CHOP or vice versa in any sub-group.

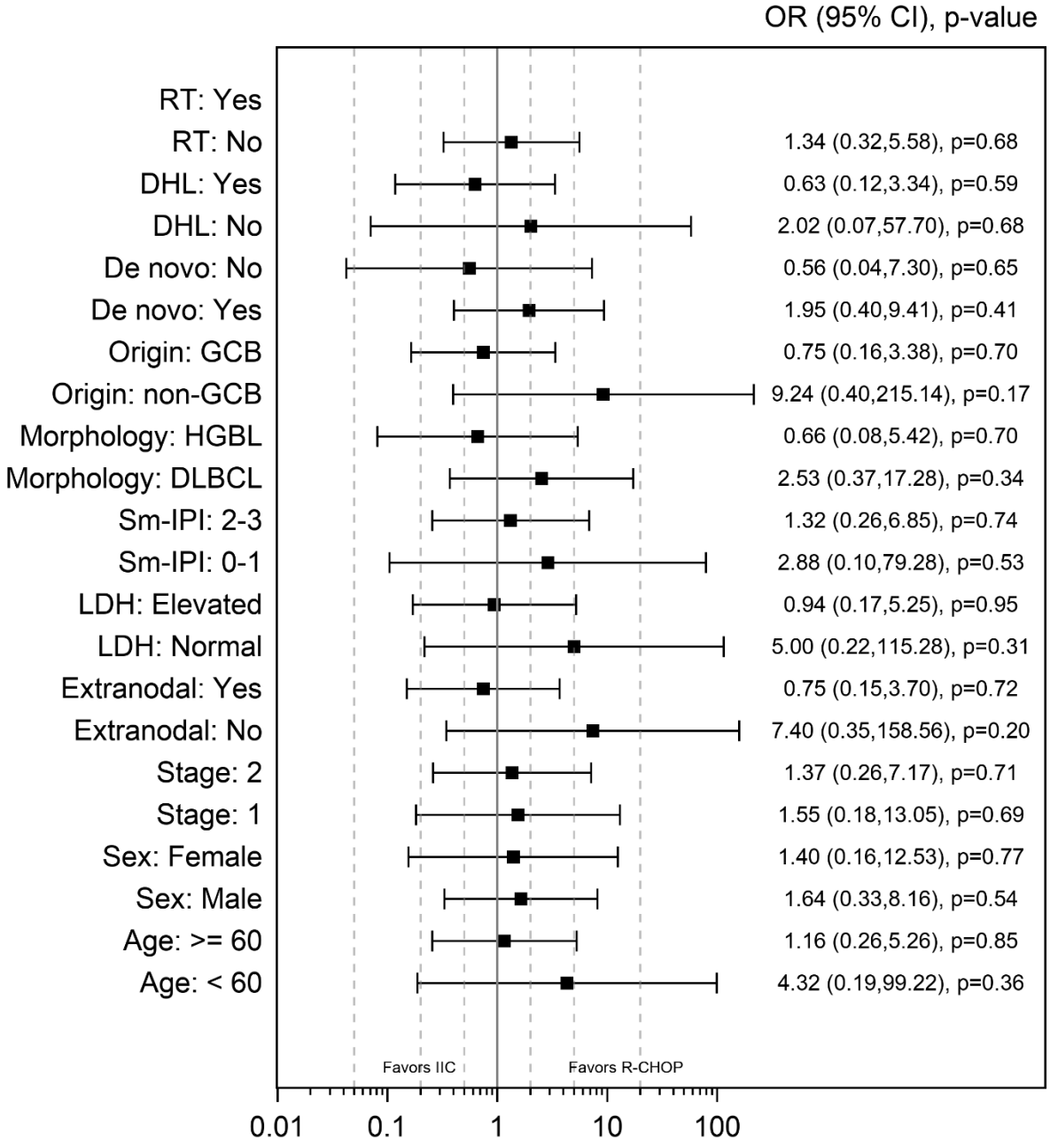


Figure 1c. Forrest plot comparing PFS in the R-CHOP vs IIC group stratified by various baseline parameters. There was no benefit of IIC over R-CHOP or vice versa in any sub-group.

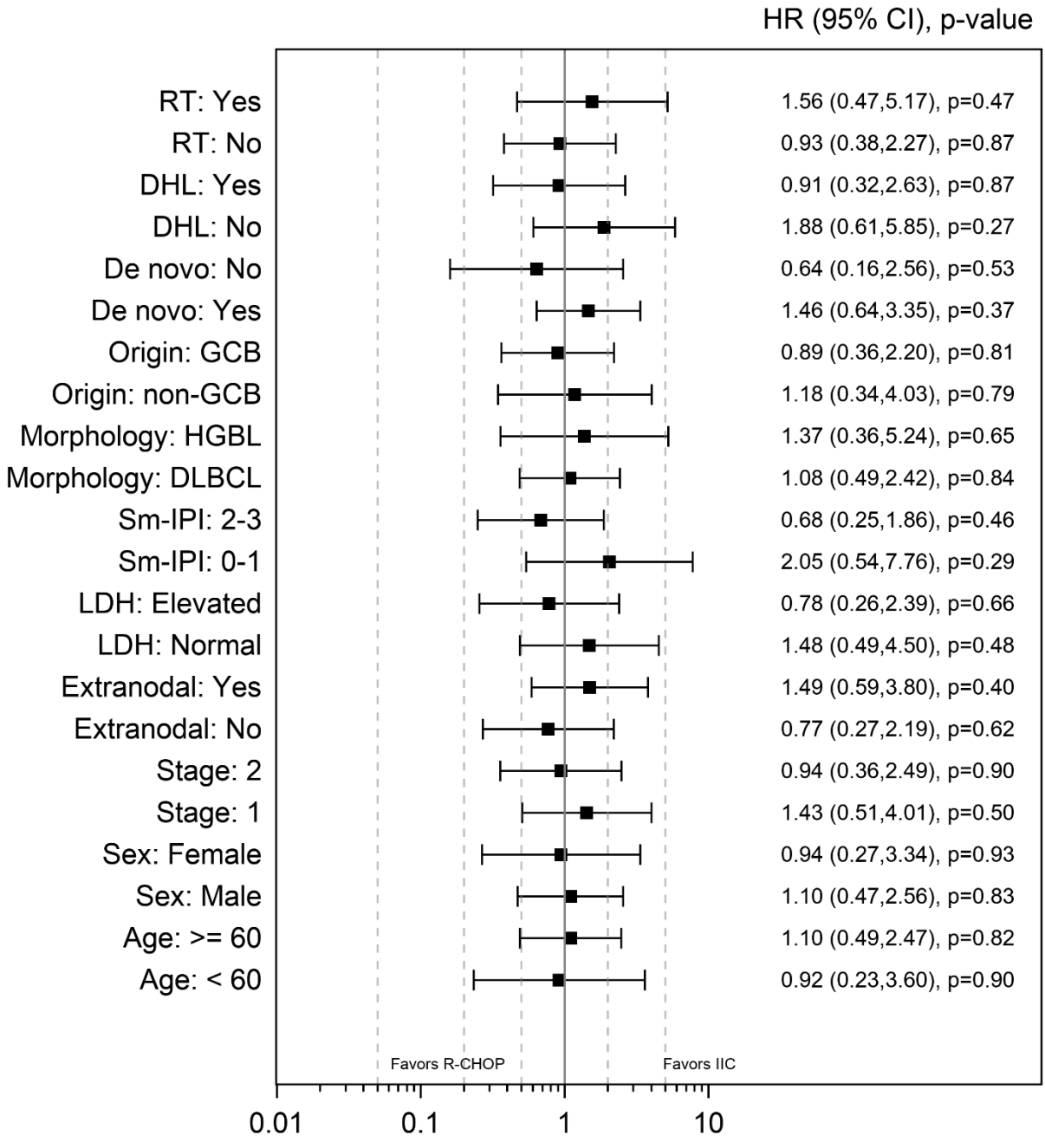
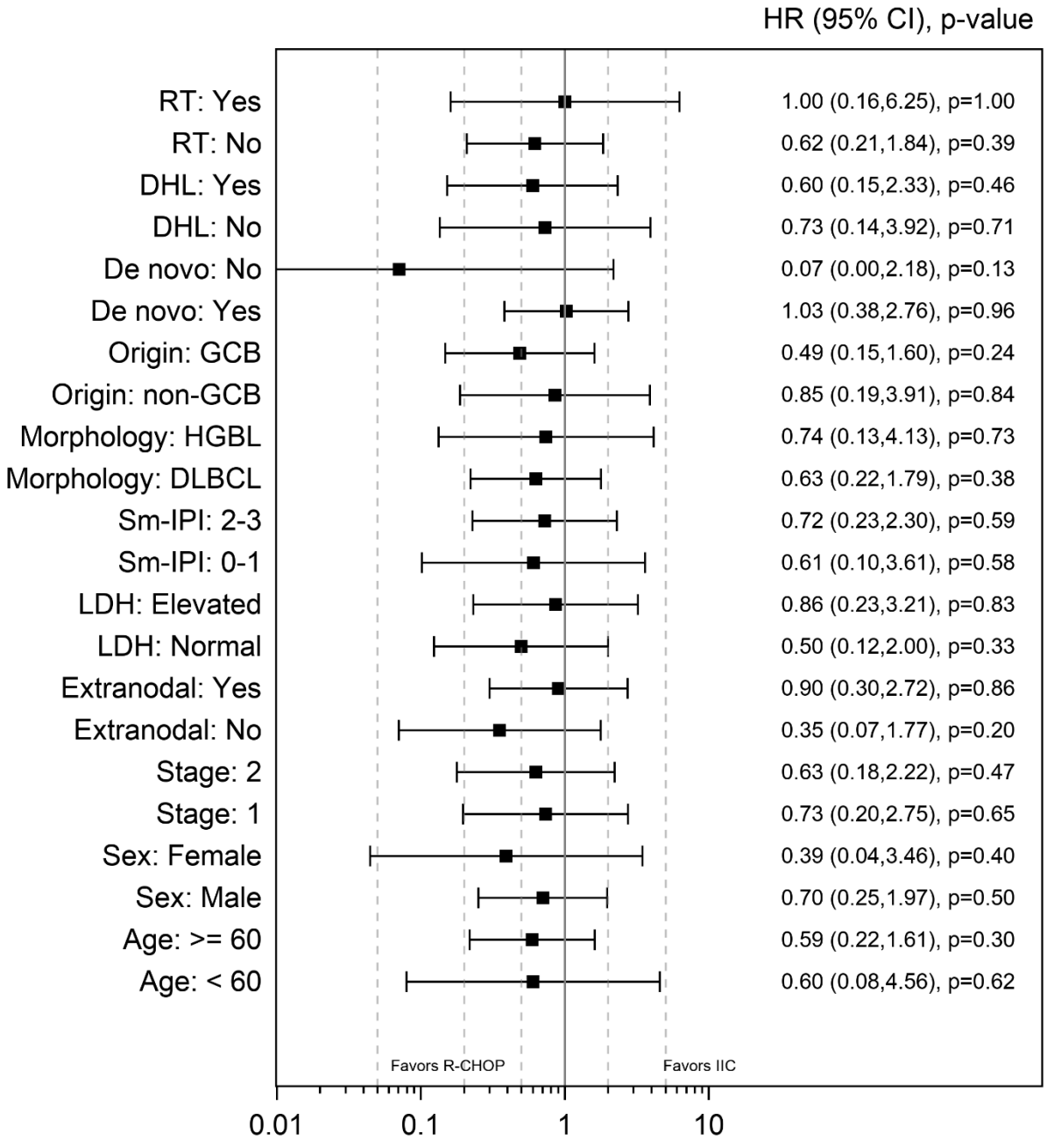


Figure 1d. Forrest plot comparing OS in the R-CHOP vs IIC group stratified by various baseline parameters. There was no benefit of IIC over R-CHOP or vice versa in any sub-group.



Figures 2a-d. Forrest plots comparing R-CHOP vs IIC stratified for various baseline characteristics in the DHL subgroup (n=40). The odds of achieving a CR were higher in patients with GCB cell-of-origin and among those who did not receive RT, however this was not reflected in ORR, PFS or OS.

Abbreviations: sm-IPI, stage modified international prognostic index; LDH, lactate dehydrogenase, DLBCL, diffuse large B-cell lymphoma; HGBL, high-grade B-cell lymphoma; GCB, germinal center B-cell; DHL, double-hit lymphoma; RT, radiation therapy; CNS, central nervous system; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone; IIC, intensive immunochemotherapy.

Figure 2a. Forrest plot comparing CR rates in the R-CHOP vs IIC group stratified by various baseline parameters in the DHL cohort. Odd of achieving a CR were higher with IIC group than R-CHOP in patients with GCB cell-of-origin and among those who did not receive RT.

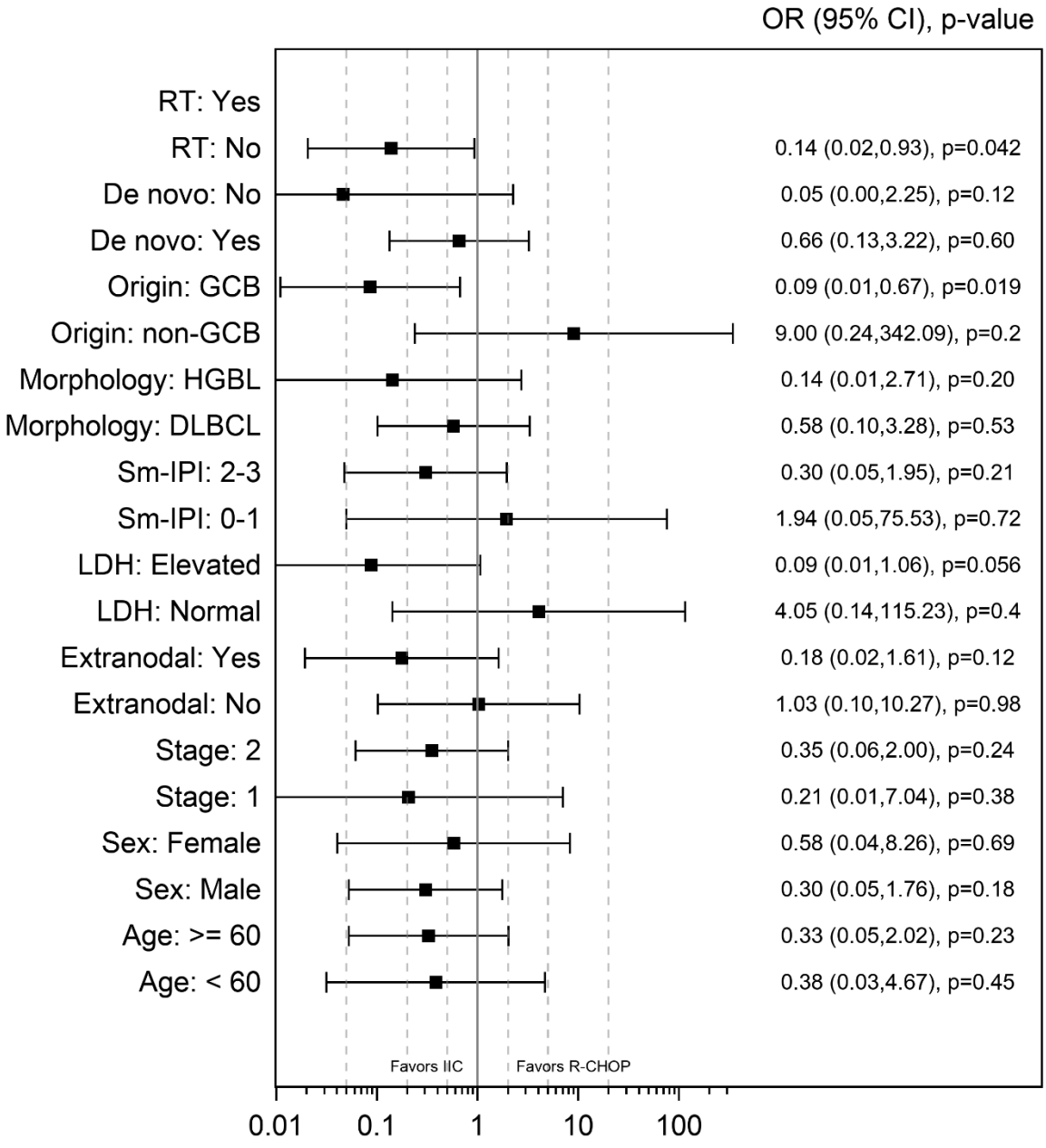


Figure 2b. Forrest plot comparing ORR in the R-CHOP vs IIC group stratified by various baseline parameters in the DHL cohort. There was no benefit of IIC over R-CHOP or vice versa in any sub-group.

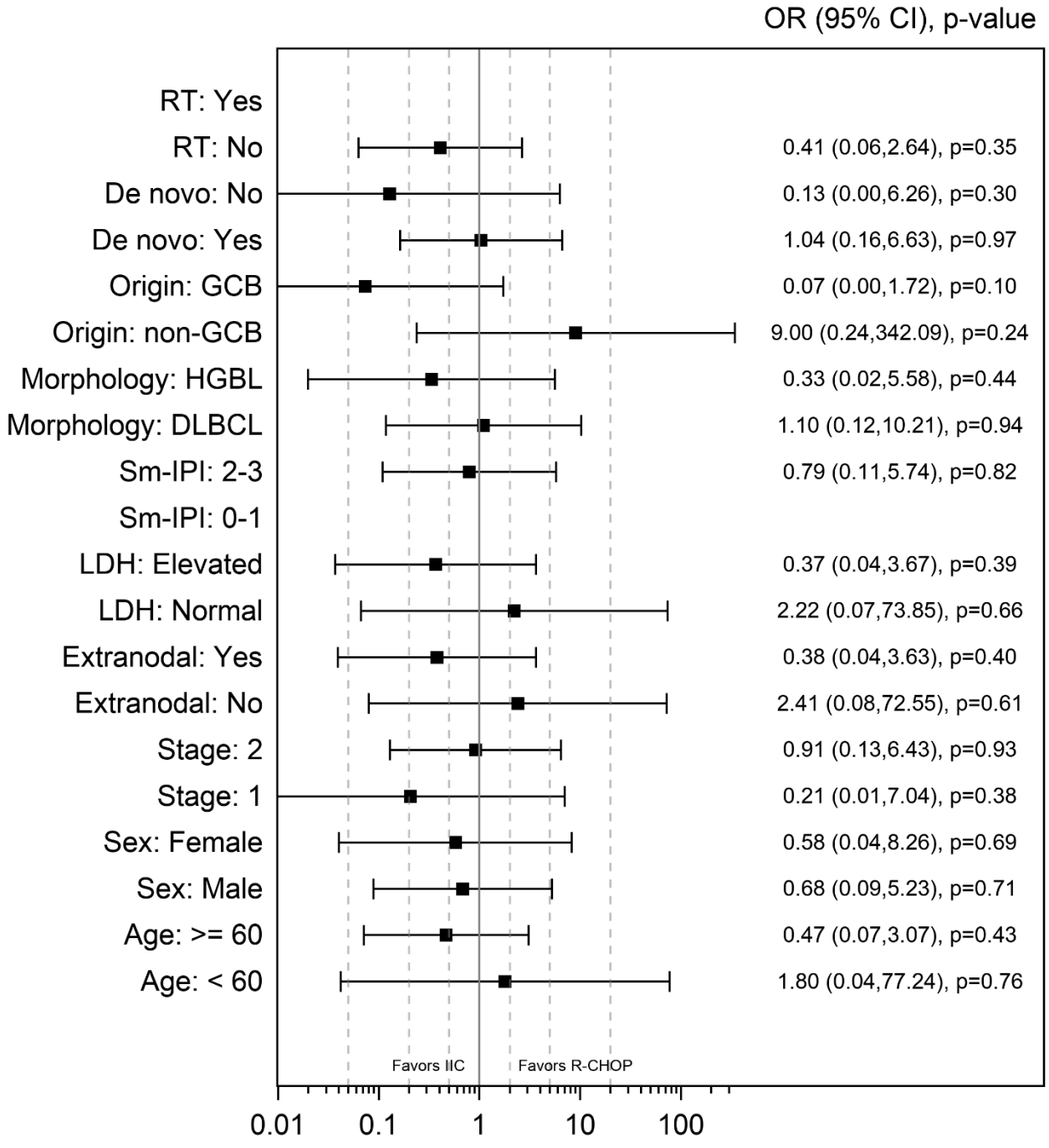


Figure 2c. Forrest plot comparing PFS in the R-CHOP vs IIC group stratified by various baseline parameters in the DHL cohort. There was no benefit of IIC over R-CHOP or vice versa in any sub-group.

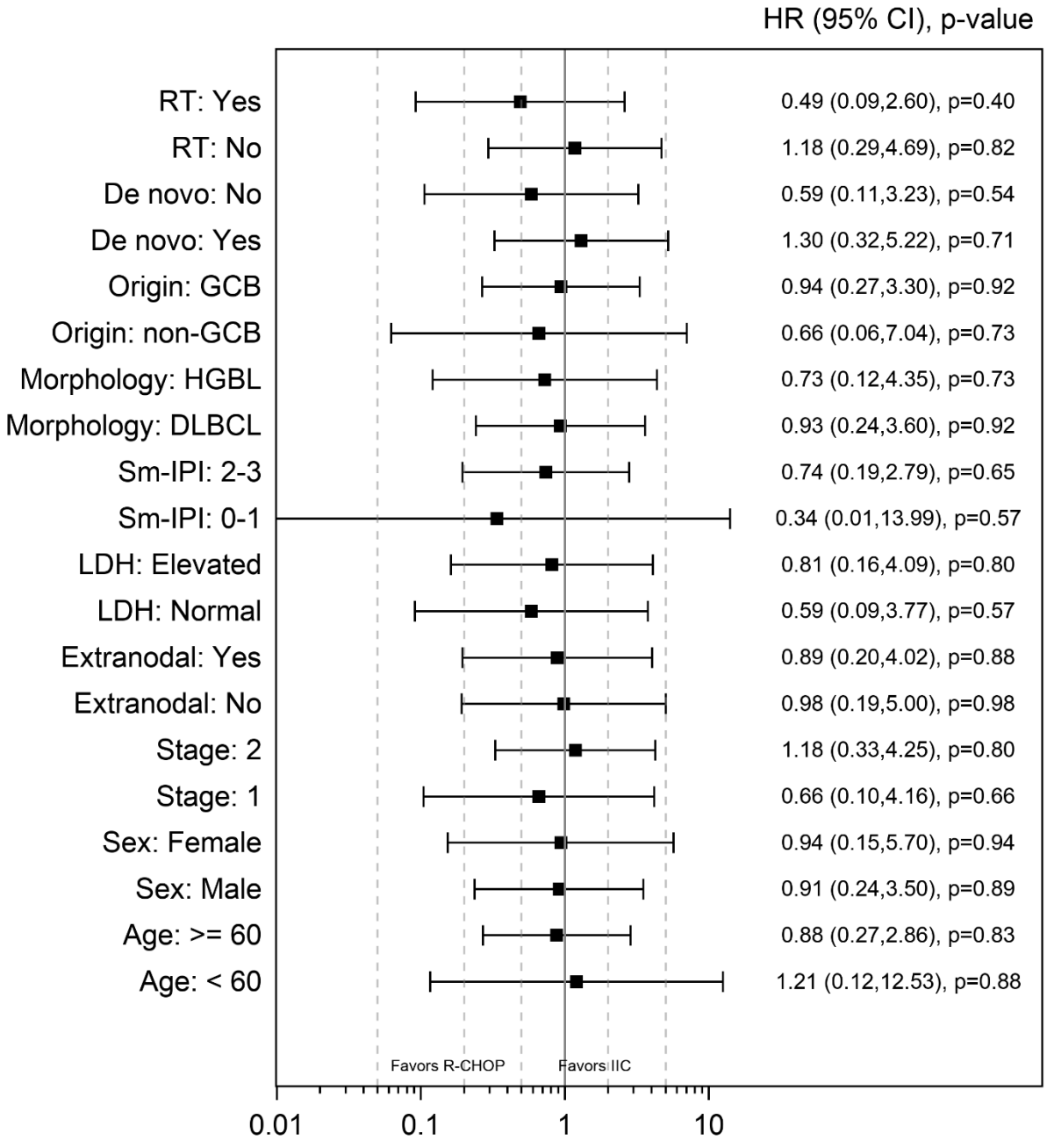
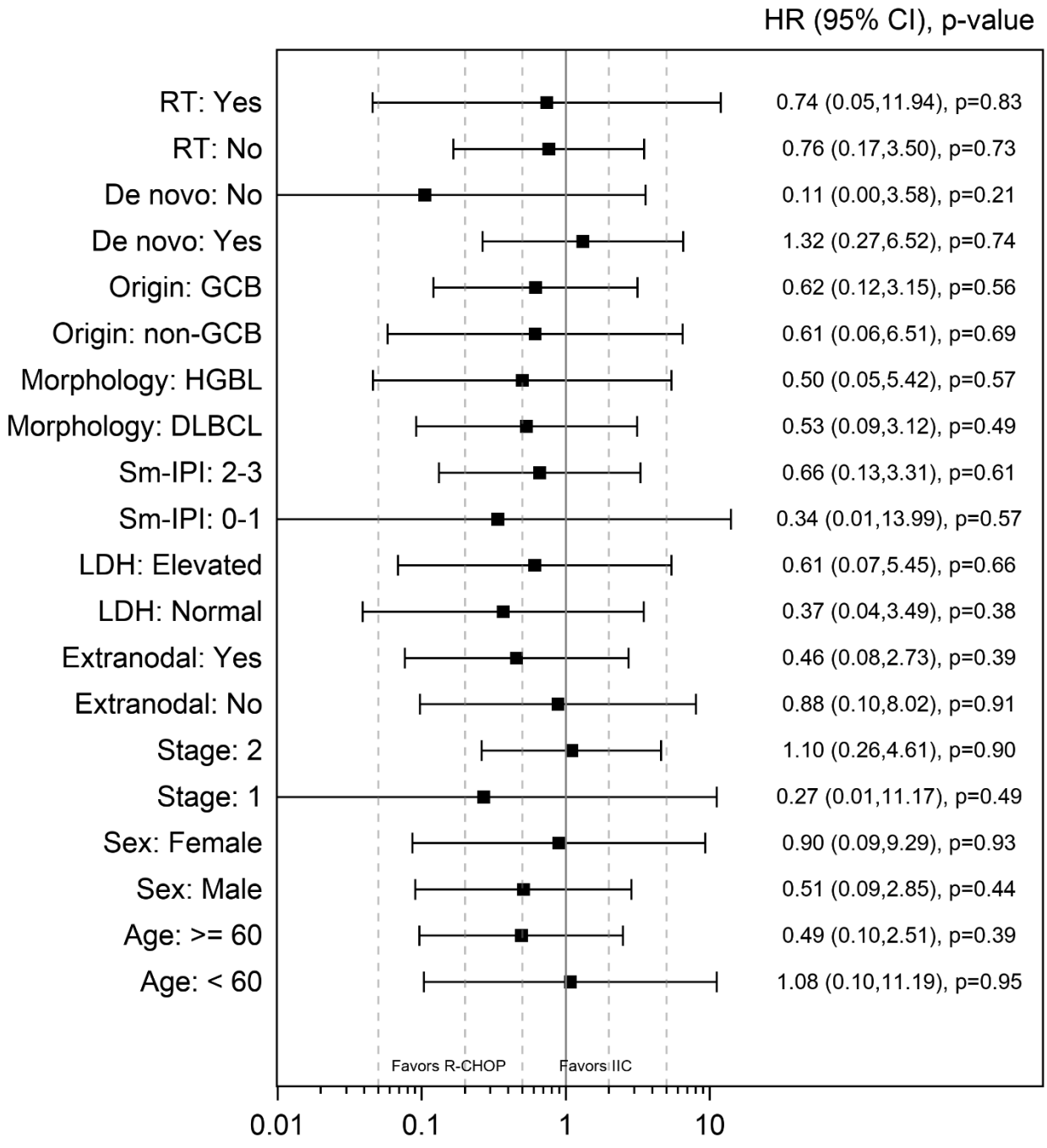


Figure 2d. Forrest plot comparing OS in the R-CHOP vs IIC group stratified by various baseline parameters in the DHL cohort. There was no benefit of IIC over R-CHOP or vice versa in any sub-group.



Supplemental Table 1. Impact of baseline prognostic factors on PFS in univariate analysis.

Variable	Level	Univariate	
		Hazard Ratio (95% CI)	p-value
Age	< 70	1.00	0.090
	≥70	1.81 (0.91, 3.59)	
Sex	M	1.00	0.82
	F	0.92 (0.46, 1.87)	
Sm-IPI	0/1	1.00	0.026
	2/3	2.32 (1.11, 4.87)	
Ki67	Unit Inc.	1.01 (0.99, 1.03)	0.42
Stage	1	1.00	0.54
	2	1.23 (0.63, 2.42)	
LDH	Normal	1.00	0.043
	Elevated	2.08 (1.02, 4.24)	
Extranodal	no	1.00	0.93
	yes	1.03 (0.52, 2.03)	
Histology	DLBCL	1.00	0.12
	HGBL	1.84 (0.86, 3.94)	
Cell of Origin	non-GCB	1.00	0.44
	GCB	0.75 (0.37, 1.54)	
Low Grade Transformation	no	1.00	0.019
	yes	2.42 (1.16, 5.08)	
# Cycles	< 6	1.00	0.99
	≥ 6	1.01 (0.51, 2.01)	
RT	no	1.00	0.75
	yes	0.90 (0.45, 1.81)	
CNS Prophylaxis	no	1.00	0.25
	yes	0.62 (0.27, 1.40)	
Double Hit Status	no	1.00	0.66
	yes	1.18 (0.56, 2.51)	
B Symptoms	no	1.00	0.70
	yes	0.83 (0.32, 2.15)	
MYC Expression	<40%	1.00	0.96

	>=40%	1.04 (0.27, 4.04)	
BCL2 Expression	<50%	1.00	0.078
	>=50%	2.69 (0.90, 8.06)	
Regimen	R-CHOP	1.00	0.79
	IIC	0.92 (0.46, 1.83)	

Abbreviations: sm-IPI, stage modified international prognostic index; LDH, lactate dehydrogenase, DLBCL, diffuse large B-cell lymphoma; HGBL, high-grade B-cell lymphoma; GCB, germinal center B-cell; DHL, double-hit lymphoma; RT, radiation therapy; CNS, central nervous system; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone; IIC, intensive immunochemotherapy.

Supplemental Table 2. Impact of baseline prognostic factors on PFS in multivariate analysis

Model	Variable	Level	Multivariate	
			Hazard Ratio (95% CI)	p-value
1	RT	No	1.00	0.69
		Yes	1.18 (0.52-2.67)	
	CNS prophylaxis	No	1.00	0.41
		Yes	0.68 (0.27-1.71)	
	Treatment	R-CHOP	1.00	0.76
		IIC	1.16 (0.45-2.98)	
2	Age	< 60	1.00	0.36
		≥60	1.51 (0.62, 3.70)	
	DHL	No	1.00	0.90
		Yes	1.05 (0.48, 2.28)	
	Treatment	R-CHOP	1.00	0.70
		IIC	0.86 (0.40, 1.87)	
3	Transformed	No	1.00	0.10
		Yes	2.22 (0.86, 5.74)	
	DHL	No	1.00	0.88
		Yes	0.94 (0.41, 2.16)	
	Treatment	R-CHOP	1.00	0.48
		IIC	0.76 (0.35, 1.63)	
4	Age	<60	1.00	0.36
		≥60	1.44 (0.66, 3.15)	
	Transformed	No	1.00	0.031
		Yes	2.32 (1.08, 4.97)	
	Treatment	R-CHOP	1.00	0.69
		IIC	0.87 (0.43, 1.74)	

Abbreviations: RT, radiation therapy; CNS, central nervous system; DHL, double hit lymphoma, R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone; IIC, intensive immunochemotherapy.

Supplemental Table 3. Impact of baseline prognostic factors on OS in univariate analysis

Variable	Level	Univariate	
		Hazard Ratio (95% CI)	p-value
Age	< 70	1.00	0.001
	≥70	4.06 (1.72, 9.61)	
Sex	M	1.00	0.47
	F	0.72 (0.29, 1.75)	
Sm-IPI	0/1	1.00	0.025
	2/3	2.80 (1.14, 6.91)	
Ki67	Unit Inc.	1.01 (0.98, 1.04)	0.45
Stage	1	1.00	0.69
	2	1.18 (0.52, 2.68)	
LDH	Normal	1.00	0.078
	Elevated	2.15 (0.92, 4.99)	
Extranodal	no	1.00	0.34
	yes	1.52 (0.64, 3.59)	
Histology	DLBCL	1.00	0.23
	HGBL	1.76 (0.69, 4.48)	
Cell of Origin	non-GCB	1.00	0.42
	GCB	0.71 (0.31, 1.65)	
Low Grade Transformation	no	1.00	0.38
	yes	1.54 (0.59, 3.99)	
# Cycles	< 6	1.00	0.79
	≥ 6	0.90 (0.39, 2.06)	
IFRT	no	1.00	0.31
	yes	0.64 (0.26, 1.56)	
CNS Prophylaxis	no	1.00	0.97
	yes	0.98 (0.34, 2.85)	
Double Hit Status	no	1.00	0.42
	yes	1.49 (0.57, 3.95)	
MYC Expression	<40%	1.00	0.34
	>=40%	2.87 (0.33, 25.08)	
BCL2 Expression	<50%	1.00	0.21

Variable	Level	Univariate	
		Hazard Ratio (95% CI)	p-value
	>=50%	2.26 (0.63, 8.10)	
Regimen	R-CHOP	1.00	0.28
	IIC	1.65 (0.67, 4.07)	

Abbreviations: sm-IPI, stage modified international prognostic index; LDH, lactate dehydrogenase, DLBCL, diffuse large B-cell lymphoma; HGBL, high-grade B-cell lymphoma; GCB, germinal center B-cell; DHL, double-hit lymphoma; RT, radiation therapy; CNS, central nervous system; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone; IIC, intensive immunochemotherapy.

Supplemental Table 4. Impact of baseline prognostic factors on OS in multivariate analysis

Model	Variable	Level	Multivariate	
			Hazard Ratio (95% CI)	p-value
1	RT	No	1.00	0.95
		Yes	1.03 (0.37-2.91)	
	CNS prophylaxis	No	1.00	0.93
		Yes	1.05 (0.32- 3.44)	
	Treatment	R-CHOP	1.00	0.81
		IIC	1.16 (0.33-4.07)	
2	Age	<60	1.00	0.39
		≥60	1.69 (0.51, 5.58)	
	DHL	No	1.00	0.66
		Yes	1.26 (0.45, 3.53)	
	Treatment	R-CHOP	1.00	0.31
		IIC	1.72 (0.60, 4.91)	
3	Transformed	No	1.00	0.82
		Yes	1.14 (0.35, 3.79)	
	DHL	No	1.00	0.44
		Yes	1.50 (0.53, 4.20)	
	Treatment	R-CHOP	1.00	0.42
		IIC	1.53 (0.55, 4.29)	
4	Age	<60	1.00	0.13
		≥60	2.15 (0.80, 5.81)	
	Transformed	No	1.00	0.54
		Yes	1.35 (0.51, 3.54)	
	Treatment	R-CHOP	1.00	0.25
		IIC	1.71 (0.69, 4.21)	

Abbreviations: RT, radiation therapy; CNS, central nervous system; DHL, double hit lymphoma, R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone; IIC, intensive immunochemotherapy.